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EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT PAPER NUMBER

1634

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/033,244

Applicant(s)

BOTSTEIN ET AL.

Examiner

Jeffrey Fredman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-27 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 22-27 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____.

DETAILED ACTION

Priority

The current application is denied priority to PCT/US/99/28551 and the various provisional applications cited because a sequence search by the STIC did not find matches to SEQ ID NO: 2 in these applications. If, in fact, the sequences were present in the applications, but they did not comply with sequence rules, (or were missed for some other reason) Applicant is requested to specifically identify by page and line number the location of the sequences. Applicant is also requested to specifically identify any substantial and specific utilities present in these priority applications.

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 22-27 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of antibodies which bind to a protein termed PRO1800 in the specification.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The cited utilities in the specification are that the protein is related to the Hep27 protein,

which the specification states may be involved in some DNA synthesis related pathway. There is some evidence of overexpression in certain lung tumors (but not in others) at page 117. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the protein. No well established utilities for this specific PRO1800 protein, antibody or nucleic acid are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, the evidence in the specification provided is that the protein is related by homology to the Hep 27 protein. This relationship lacks any of the hallmarks of utility. The homology does not imply that the proteins are similar in any function way, or that they are expressed in similar tissue types or under similar conditions. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner or any other specific feature which is disclosed as being associated with PRO1800. Without any further information, there is no expectation that the protein will have any properties in common with the Hep 27 protein. There is an abundance of evidence that very similar proteins can perform very different functions. For example, Rost et al (J. Mol. Biol. (2002) 318(2):595-608) notes regarding assignment of enzymatic activity based upon homology comparisons that "The results illustrated how difficult it is to assess the conservation of protein function and to guarantee error-free genome annotations, in general: sets with millions

of pair comparisons might not suffice to arrive at statistically significant conclusions (abstract).” Thus, even high levels of homology do not necessarily correlate with actual protein function. In the current case, where not only is the function of PRO1800 not known, but no specific function has been definitively identified for the related Hep 27 protein itself, the expectation is even lower that there is any utility that can be derived based upon this association.

As noted in the utility guidelines, basic research on a product to identify properties and intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). First, there is NO data in the specification showing association of PRO1800 with any disease state.

Second, the overexpression data does not provide a substantial utility for several reasons. First, there is no showing that the overexpression was statistically significant and correlated with any diagnostic utility. The absence of such a diagnostic utility is particularly striking since there is no evidence that the overexpression effect was statistically significant, that the effect was reproducible, or that the effect was anything other than a nonspecific effect due to the presence of an exogenous protein in the mixture.

Specific Utility

In the current case, even if the substantial utility argument above were found unpersuasive, there is no specific utility given for this protein and resultant nucleic acid. The protein has not been associated with any disease, any condition, any enzymatic

activity or any other specific feature. The only association is that it has some homology to a protein, Hep 27, which is associated with DNA synthesis in some undefined way. As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". Here, there is no disclosure of any condition which can be diagnosed and hence, no specific utility.

Finally, with regard to the utility analysis, the current situation directly tracks Example 4 of the utility guidelines, where a protein of entirely unknown function was characterized as lacking utility.

Claim Rejections - 35 USC § 112 – Scope of Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 22-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention

The claims are drawn to antibodies which bind the PRO1800 protein. The invention is in a class of invention which the CAFC has characterized as “the unpredictable arts such as chemistry and biology.” *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass any antibody which binds to the PRO1800 protein and also include any antibody fragments which bind to the PRO1800 protein.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the activity of polypeptides and antibodies. It would require significant study to identify the actual function of the PRO1800 protein, and identifying a use for this protein would be an inventive, unpredictable and difficult undertaking in itself. This would require years of inventive effort, with each of the many intervening

steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art is extremely unpredictable with regard to protein function in the absence of reliable information regarding the protein activity. Even very similar proteins, as shown by homology, may have very different functions (see Rost et al (J. Mol. Biol. (2002) 318(2):595-608). In the current case, where no specific information is known regarding the function of the protein in actual biological organisms, it is entirely unpredictable what function and activity will be found for this protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the protein.

Working Examples

The specification has one working example in which the nucleic acid may be overexpressed in some tumor samples, but the working example lacks sufficient information regarding internal controls to show that the protein was, in fact, overexpressed, that the nucleic acid was associated with any disease or that the results are anything other than spurious.

Guidance in the Specification.

The specification, while correlating PRO1800 with Hep 27, did not teach any actual function or use for PRO1800, nor, in fact, any use for Hep 27 itself.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 22-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Bandman et al (WO 00/04135).

As noted in the priority section above, this application is currently granted priority only to parent application 09/866,034, filed May 25, 2001, and not to PCT/US99/28551 or the provisional applications regarding the claimed subject matter because the sequences were not found in the sequence search in the PCT. If there is priority, Applicant is requested to identify the basis of the support by application number, page

and line number and also identify supporting utilities found in the same specification by page and line number.

Bandman teaches synthesizing antibodies to the SCRM protein (see page 47, lines 15-30). The SCRM protein has 96% local similarity (see attached alignment) with SEQ ID NO: 2. It is inherent that antibodies to the Bandman SCRM protein would also interact with SEQ ID NO: 2. In particular, the peptide antibodies would nearly all share identical peptide target sequence, resulting in identical antibody specificity (see page 47, lines 24-30). Bandman further teaches formation of monoclonal antibodies as required by claim 23 (see page 27, lines 11-16) and chimeric or humanized antibodies as required by claim 24 (see page 27, lines 17-25). Band further teaches antibody fragments as required by claim 25 (see page 27, lines 30-35). Finally, Bandman teaches labeling as required by claim 26 (see page 23, lines 7-19).

Conclusion


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman
Primary Examiner
Art Unit 1634

May 1, 2003